(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) Publication number: **0 280 418 A1**

B4

(12) **EUROPEAN PATENT APPLICATION**

(21) Application number: 88300882.3

(51) Int. Cl.4: **A61B 5/00 , G01N 21/47**

(22) Date of filing: 02.02.88

(30) Priority: 02.02.87 US 9447

(43) Date of publication of application: 31.08.88 Bulletin 88/35

(84) Designated Contracting States: DE FR GB IT SE

(71) Applicant: WYATT TECHNOLOGY CORPORATION
820 East Haley Street
Santa Barbara California 931030(US)

(72) Inventor: Wyatt, Philip J.
82o East Haley Street P.O. Box 3003
Santa Barbara, CA 93130(US)

(74) Representative: Godsill, John Kenneth
Haseltine Lake & Co. Hazlitt House 28
Southampton Buildings Chancery Lane
London WC2A 1AT(GB)

(54) **Method and apparatus for examining the interior of semi-opaque objects.**

(57) A highly collimated light beam, such as produced by a laser (1), is coupled by optical means (2,3,4,5) directly onto a semi-opaque object (21) such as a human breast. The light transmitted and scattered therein is collected at a fixed surface element and direction relative to the incident light, and coupled optically into an image intensifier (10) preserving th spatial intensity variations passing through said fixed surface element. The intensified image is then collected on an array of detector elements (13) which digitizes and then transfers said preserved image into memory means where it is processed to characterize the interior of said object.

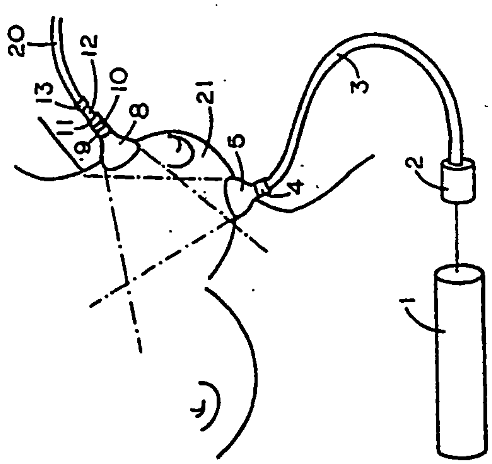

FIGURE 3

EP 0 280 418 A1

METHOD AND APPARATUS FOR EXAMINING INTERIOR OF SEMI OPAQUE OBJECTS

This invention relates to a method and apparatus for examining the interior of semi-opaque objects. This invention has particular application for the early detection of breast cancer, a screening procedure most frequently performed x-ray means (mammography), light transmission (diaphonography), thermal imaging (thermography), and ultrasound.

The non-invasive examination of the interior of materials has been a familiar procedure for many years. This is particularly true for the radio-logical examination of human tissues using x-ray sources. Many such x-ray techniques have been improved significantly in recent years, both as regards safety and resolution. Safety has been increased by means of greatly improved films, permitting dramatic reductions of radiative doses and the risks associated with exposure to x-rays. Applied to the detection of breast cancer, x-ray examination (mammography) is considered the standard and most successful procedure for detecting early signs of disease, despite a false negative rate often exceeding 20%. False positive results often equal or exceed true positive results.

Another method for detecting breast cancer uses transmission spectroscopy where a bright, quasi-monochromatic light emitter is placed in proximity to the breast surface, and a television recording or digital image is made of tissue illuminated by the light transmitted through it. A similar scan is made at a slightly different wavelength, and the two images are combined by means of an enhancement algorithm. The final image is then examined by a trained interpreter who makes estimates as to probable carcinoma of disease based on various absorption criteria. Such instruments are of the type sold under the tradename "Spectrascan Model 10" manufactured by Spectrascan, Inc. Once again, for this procedure the false negative rate often exceeds 25%, even with a trained interpreter, and false positive rates may be very high.

Mammography, spectral transmission, and ultrasound are often used in conjunction with one another as a means of detecting carcinomas and other lesions by one method when not detected by another. Ultrasound techniques are used primarily to detect nodules or smaller non-palpable masses. It is in the hope of detecting the onset of carcinomas before they are detected by ultrasound that mammography and spectral transmissions have held their greatest promise, yet their most successful applications also have been for the detection of small, non-palpable masses. The combination of methods still produces an unacceptably high level of false negative (and positive) results.

The relatively high levels of false positives referred to above and associated with all of the methods are perhaps even more distressing than the high incidence of false negative results. If all examinations by a certain technique were classified as positive (on the basis of a given screening technique), then the technique would be considered by its proponents as perfect, since all lesions would have been detected. But a huge number of needless biopsies would have been performed, and if every examination required a biopsy, then the screening technique itself would be useless. Girolama and Gaythorpe, in their recent CRC Critical Review (1984)of Clinical Diaphanography and related measurements (mammography, ultrasound, thermography, etc.), present data of many practitioners that show that the number of biopsies performed often exceeds <u>ten times</u> the number of true breast carcinomas found. The diagnostic procedures seem to have some utility, but hardly seem reliable. Indeed, both mammography and diaphanography, currently the most reliable procedures, seem incapable of detecting deep lesions smaller than about 2 mm in diameter.

Since the <u>interpretation</u> of both mammographs and diaphanographs requires trained interpreters, and such training in itself requires a phenomenological correlation between things "seen" and carcinomas discovered by biopsy or other surgical procedure, one should ask the question: Is the information disclosed consistent with the measurement made?

In the case of x-rays (mammography), the uncomfortable and often painful examination procedure requires, for its most useful application, that the examined breast be compressed to make it more uniformly thick to yield "even penetration by the x-rays, less difference in radiographic density of the chest wall area and the nipple, and reduced radiation dose...." (Girolama and Gaythorpe, <u>loc. cit</u>.). Yet, as has already been mentioned, the ability of such measurements to identify early true carcinomas remains very low. Light transmission measurements seem to yield even worse results. Mammograms disclose differences in the absorption of x-rays by various tissues constituents, yet there are many sources for transmission differences that are unrelated to carcinomas of the breast. It is only by <u>training</u> and <u>experience</u> that mammograms may be interpreted properly. But if we seek to detect an abberant cellular morphology of some endothelial cells whose extent is often only tens of micrometers, are x-rays whose wavelength are a few nanometers are most suitable radiation source? The mismatch of the wavelength of x-rays

with the size of cancerous cells would suggest not. However, the ability of x-rays to penetrate through otherwise opaque material suggests some vague utility for detecting cumulative abberant absorptions of layers upon layers of diseased cells. A nodule of two millimeters diameter detected by x-ray means and confirmed by subsequent biopsy is surely a well-developed carcinoma rather than an early manifestation of cancer. By the time x-ray techniques detect such lesions, the corresponding carcinoma is probably a later manifestation of disease. True, such detection is often earlier than detection by palpation alone and can improve survival statistics, but it surely cannot be called "early detection" which must occur at the cellular level, i.e. at the first occurrence of a cancerous cell. This "early detection" misnomer persists among proponents of mammography.

Light transmission of diaphanographic methods have similar problems. Although light wavelengths in the near infrared provide a better match to the size of mammalian cells, or at least the regions within cells where the cancerous state is confirmed by cytological examination, the tremendous scattering and attenuation of light by tissue makes it difficult, at best, to develop consistent deductions of probable lesions, especially deep in the tissue. Because of the multiple scattering of light within tissue, the detected signals are degraded and accordingly must carry very little information with them about the environment deep within the tissue. The most "spectacular" observations achieved by light transmissions and its variants have been the graphical disclosures of near surface phenomena and features such as veins, implants, cysts, nipple regions, etc.

In reviewing the literature describing the x-ray and light measuring techniques for the early detection of breast cancer, I have become aware of a new approach and instrumentation by which light may be used to yield more significant information about the sources of its scattering during its traversal of the breast. Although my discussion has centered primarily upon applications relating to the detection of breast cancer, it will be obvious to those skilled in the art that the method and apparatus may be applied equally well to other tissue, as well as semi-opaque objects not so-related.

According to one aspect of the invention, there is provided a method of examining the interior of a semi-opaque object with light, the method comprising:

coupling a collimated beam of light to a first surface portion of said body;

collecting light scattered within said body at a further surface portion of the body;

amplifying the collected light whilst substantially preserving its spatial intensity variations;

converting pixels of the amplified light into electrical data signals which are passed to computer means for storage therein;

processing the resulting data in the computer means to characterise the region of the object causing spatial variations in the collected light;

repeating the processing for different orientations of the incident and/or collected light.

According to another aspect of the invention there is provided an instrument for the examination of the interior of a semi-opaque object and comprising:

collimated light generating means for providing a beam of light for coupling to an entrance surface of said object; and

light collection and processing means for collecting light from said beam which has scattered within the body and emerged from an exit region thereof;

characterised in that the collection and processing means comprise collection optical fiber means for coupling by refractive index matching means to said exit region, light amplification means for amplifying light from said collection optical fiber means while maintaining its spatial variations at said collector optical fiber means, photodetector array means for converting pixels of the amplified light to electrical signals, analog-to-digital conversion means for converting said signals to digital form, and computer processing means for storing and processing said signals in digital form.

According to a further aspect of the invention there is provided an apparatus for producing a near parallel, spatially homogeneous, unpolarized laser beam from a spatially inhomogeneous laser beam, comprising a half pitch gradient refractive index lens joined on its central axis to an optical fiber which, in turn, is joined to substantially identical gradient refractive index lens

One embodiment comprises eight basic interacting elements: 1) a monochromatic, highly collimated, polarized or unpolarized light source which preferably will be a continuous or pulsed laser operating in the red or near infrared spectrum; 2) an optical transmission means, such as a fused and highly polished, flaired, optical fiber bundle by which the light so-generated is brought to the surface of the semi-opaque object to be examined; 3) a coupling fluid that eliminates any air interface between the transmission means and the object being illuminated; 4) an optical collection means located at a different position on the object and equivalently coupled by fluid means to the object transmitting the light incident thereon; 5) transmission means by which light collected by said collection means is transmitted to 6) a very high gain light amplification means that preserves the spatial distribution of intensity levels incident before am-

plification; 7) a high resolution detection means comprising a two-dimensional array of detector pixels that again preserve the spatial distribution of the amplified light intensities incident thereon, and providing signals to 8) storage, display, and computer means.

In this manner, the light coupled into the object to be examined is well-defined in terms of its wavelength, polarization, and incident direction. Reflections at the object surface are minimized by inserting an index matching fluid between the light transmission means and the object. Transmitted light is then removed at a specific angle/position on the object with respect to the direction/position of the incident light, with a similar index matching fluid between the object and collector means. It is important to note that the direction of the collected transmitted light is not generally along the line of the incident radiation. A high resolution detector follows an image intensifier to yield a detailed image of the emerging light at the object surface.

For a better understanding of the invention and to show how the same may be carried into effect, reference will now be made, by way of example, to the accompanying drawings, in which:

Figure 1 shows an embodiment of a transmitter device comprising an incident light source coupled by optical fiber means into a flaired, and fused, concave optical bundle;

Figure 2 presents a similar view of a collection device comprising a flaired optical bundle light collection means fused to a faceplate of an image intensifier whose output signal is coupled into a self-scanned CCD array which, in turn, supplies signals to a video display and a computer means;

Figure 3 shows a typical placement of the device of Figure 1 during breast examination;

Figure 4 shows the interface between an object and the device of Figure 1 or 2 with an index matching fluid therebetween ;

Figure 5 shows a fine array of gradient refractive index lenses, each attached to discrete fibers,

Figure 6 shows the optical axis of transmitter and collector means of the devices of Figures 1 and 2, their region of intersection, and relative motions therebetween; and

Figure 7 shows a modification of the device of Figure 2 with an added lens structure producing an intensified image at detection means of scattering elements within an object.

Unlike conventional diaphanographic techniques whereby light is transmitted through the semi-opaque object and, upon emergence therefrom, is photographed or otherwise recorded by means solely of the transmitted light, the image produced by the equipment to be shortly described is created by transferring light at the surface directly to detection and recording means before such light may be diffused or defocussed by said surface. In addition, the method to be described emphasizes the detection of light scattered within the object into a specific angular direction with respect to the direction of the incident illumination. Another aspect to be discussed is the making use of a measure of the coherence of the scattered light after scattering so that the degree of internal degradation may be quantified and correlated with the angle of scattering and the distance through the intervening material it has traveled from time of injection to time of detection.

An important element of the equipment to be described is the incorporation of light amplification means into the detection means to permit use of modestly low incident laser power levels as well as to compensate for the huge losses that may well occur within the object itself. Such light amplification means may be controlled so that the overall gain of the system may compensate for differences in optical path lengths of the examined structures.

It will be appreciated by those skilled in the art of light transmission measurements that this invention provides far greater detail of the transmission and scattering processes occurring within the object than has been attainable hitherto. Accordingly, my invention will find great utility in the interpretation and explanation of the structural elements of the semi-opaque object itself, but, like other methods, will require a new set of phenomenological correlations of the new information disclosed with the results of invasive examination.

It is now explained in detail how the preferred embodiment yields an instrument of exceptional sensitivity for the examination of the interior of semi-opaque objects. Since the most important application of this embodiment will be in the area of cancer detection within a human breast, it will be illustrated by frequent reference thereto.

Figure 1 presents a view of the key elements of a transmitter device, providing an illumination system. A laser 1 or similar light source produces a plane polarized, circularly polarized, or unpolarized monochromatic, highly collimated light beam which impinges upon a lens element 2 coupled to a long flexible optical fiber means 3. The laser produces monochromatic light of red or near infrared wavelengths between, say, 600 and 4000 nm, and produces on the average a beam power of the order of 10 to 100mW. The laser may be operated continuously, or pulsed, or even have its beam chopped. Pulsed or chopped operation can simplify some dark offset measurements and signal processing procedures performed later, though such beam interruptions are by no means essential. A He-Ne laser operating at 632.8 nm of the type manufactured by Melles-Griot or Jodan Laser

would be a reasonable choice in the red wavelengths whereas a He-Ne laser operating in the infrared at 1150 nm or 3390 nm of the type manufactured also by Jordan Laser would suffice for the infrared wavelength. The actual choice of the most suitable infrared wavelength will depend on the properties of the object being examined. Human tissue has a high water content and, therefore, sources emitting at the characteristic absorption bands of water should be avoided. The lens element 2 focuses the beam (of nominal 1mm diameter) onto the optical fiber element 3, which may preserve the polarization of the beam or destroy all memory of polarization. The lens may be of conventional structure or a half pitch gradient refractive index (GRIN) lens of the type produced by Nippon Sheet Glass Co., Ltd. under the tradename "SELFOC". The optical fiber element 3 is terminated at the focal point of another lens or GRIN lens 4 to produce a nearly parallel output beam. This, in turn, may be coupled optionally into a flaired optical bundle 5 of the type manufactured by Bausch & Lomb with a flat or slightly convex surface 6 that is brought in contact with the semi-opaque object to be examined. The terminal fiber elements of the flaired optical bundle 5 alternatively may be fused to a fine array of GRIN lenses of the type commonly used in compact "Xerographic" machines. Such terminations insure that the emerging light detected will be restricted to those remaining parallel to a given direction with minimal dispersion before entering the semi-opaque object. The entire transmitter device is covered and light tight, except for the small portion of optical bundle or GRIN lenses to be placed in contact with the object at a specific entrance location thereon. In this manner, all stray light contributions should be removed. Alternatively, a laser head itself may be held directly against the object with some refractive index matching fluid between the output laser mirror and the object. For safety reasons, however, some type of indirect fiber coupling may still be preferable since the laser head will be operated at a high voltage.

Figure 2 presents the key elements of the transmitted light collection device. A flaired optical fiber bundle 8 with a similarly fabricated flat or concave surface 7 is joined to the optical faceplate photocathode 9 of a microchannel plate light amplifier or image intensifier 10 of the type manufactured by Litton Electron Tube Division containing a red sensitive S-20, or equivalent photocathode 9 and a P46, or equivalent, phosphore fiber plate 11. Such image intensifiers, including their various formats of C-plates, chevron plates, or Z-plates are capable of producing photon amplifications of 10^6 or greater. An optical fiber endplate 12 is then joined to a very high resolution, two-dimensional charge coupled devices (CCD) array 13 of the type manufactured by Photometrics, having as many as 2048 $\times$ 2048 pixels. All elements are joined in optical contact using refractive index matching materials such as fluids or transparent gels of the types manufactured by R.P. Cargill Laboratories, Inc.

The microchannel plate image intensifier 10 is powered by a variable gain power supply 14. The CCD output is sent over cable 15 to an analog-to-digital converter 16A and then stored in a computer memory means 16B accessible for display on a high resolution monitor 17 or for digital image enhancement processing by a computer 18 and/or storage in rotary memory means 19.

Instead of a CCD array, which transmits the values of its pixel elements sequentially, image collection may be accomplished using a two-dimensional array of photodiodes whose output signals are sampled in parallel and held or frozen periodically while they are converted. These analog values would be multiplexed and then converted sequentially to digital representations for storage in the computer memory means or recording on rotating memory means 19.

Figure 3 shows the transmitter and collector structures in a particular orientation with respect to a female breast 21. A single cord 20 contains the CCD output cable 15 and the microchannel power cord. Note that the two flaired optical fiber faceplates 5 and 8 are each in contact with specific entrance and exit surfaces of the breast. Care is taken in establishing the contact required between the surfaces of the transmitter and collection devices with the object being examined. This is shown more clearly in Figure 4 where an index matching means 22 similar to the types made R.P. Cargill Laboratories is placed between the object 21 and the optical bundle 5. For maximum data retrieval of scattered and transmitted light, the transition from one material to the next must be coupled efficiently so that interface scattering, reflections and other losses be kept to an absolute minimum. An index matching fluid of refractive index 1.4 to 1.5 should suffice for the case of human skin or similar proteinaceous material.

Figure 5 shows the coupling of a set of optical fibers into an array of gradient refractive index lenses. These arrays are of the type frequently found in "Xerox-type" copy machines. This type of coupling permits, for half pitch GRIN elements, a highly restricted acceptance angle and field of view when light scattered from the object enters the GRIN lens which , in turn, focuses it into the optical fiber attached thereto. Conversely, if the light is transmitted from a fiber into a GRIN lens, it emerges nearly parallel. Attachment of GRIN arrays to the various optical fiber elements of the

coupling structures 5 or 8 will be useful in certain configurations when highly collimated light is required or it is necessary to restrict the detected field of view.

The coupling structures 5 and 8 of Figures 1 and 2, respectively, need not be of large extent. In the preferred embodiment of the invention in Figure 1, the GRIN lens 4 will have typically an output diameter of about 2 mm. The optical fiber bundle 5 may have a magnification of the order of $10^{\times}$, i.e. the emitting surface 6 will have a diameter of the order of 20 mm or even less.

An annoying characteristic of laser beams is their non-uniform intensity profile. If they emit in the so-called TEM_{00} mode, the profile is Gaussian. Such a non-uniform profile is of the form

$$I(r) = I_o \exp[-2(r/r_o)^2],$$

where I (r) is the intensity at a distance r from the beam axis, I_o is the axial intensity at r = 0, and r_o is the distance from axis at which the intensity has fallen to $1/e^2$ its axial value. It is well known that the spatial regularity of a laser may be randomized upon passing the beam through a multimode optical fiber. I have found that the structure 2-3-4 of Figure 1 results, for the case of multimode fiber 3, in an emerging beam at 5 that is nearly parallel, unpolarized, and uniform over a diameter approximately equal to the diameter of the GRIN lens 4. This is independent of the polarization state of the incident collimated illumination. If a completely homogeneous and parallel incident beam is required to pass through the object, then this 2-3-4 combination would be the preferred structure of the light transmitting module of Figure 1. The flaired optical fiber bundle 5 would be removed, and the GRIN lens 4 would be coupled directly into the object 21 by means of an index matching fluid layer 22 between the object 21 and the lens 4. For many applications, however, the GRIN lens 4 would be coupled into the flaired optical bundle 5 whose subsequent coupling into the object would still insure a strong forward directed beam through the object.

Prior to image enhancement processing by the computer 18 of the digital image generated from the CCD array 13 of the transmitted light from the object coupled into the collector bundle 8, it may be required to know the relative positions of the transmitter device (Figure 1), and collection device (Figure 2) relative to one another. Not only would their spatial coordinates be described, but so also the angle of scattering between the transmitter axis 23 and the collector axis 24 shown in Figure 6. With these measurements, the path lengths through the object, the region of intersection 25, and the angle of scattering 26 may be calculated. There are many means by which such coordinates and axial directions be known as will be appreciated by those skilled in the art. For example, the transmitter and collection devices may be attached to position and angle encoding means frequently employed in robotics, such as the chemical robot systems of Zymark, among many others.

As will be apparent from Figure 6, both transmitter 5 and collector 8 bundles may each be moved independently of one another. This feature implies that the interior of the object may be scanned in different manners. For example, by holding the collection bundle 8 fixed and rotating the transmitter bundle 5 along the directions indicated by 27, the features of the object along the detector axis 24 may be illuminated sequentially. Alternatively, fixing the transmitter bundle 5 and rotating the collection bundle 8 so that the centre 25 of the region of intersection remains the same would result only in the variation of angle 26 indicated. Thus the scattering properties of the region of intersection 25 as a function of scattering angle may be observed. Once the data were image enhanced, it might well be possible to identify, or at least characterize, the small inhomogeneities or particles located in this region 25 on the basis of methods developed earlier by the inventor and Quist.

As will be apparent to those skilled in the art of servo mechanisms, the transmitter bundle 5 may be controlled by mechanical means, preprogrammed to remain in contact with the object, to scan the entire volume of the object or any selected subvolume thereof. With the cooperative motion of the collector bundle 8, every element of the object may be subjected to multi-angle examination. The light transmitted through the object will undergo, in general, huge degradations as it passes through semi-opaque regions such as found in the human breast. Much of this degradation is the result of multiple scattering which prevents the collection device from receiving but small quantities of directly scattered light. It remains for image enhancement techniques to process the collected, high resolution data and enhance features degraded by such multiple scattering processes. Because the transmitter and collection bundles are not constrained to a single aspect with respect to one another, the enhancement process will be even more successful in resolving those features responsible for the major internal scattering events. Further measurement of coherence effects manifest by the quantity and size of "speckle" remaining in the collected light may be quantitated for the subsequent estimation of the degree of multiple scattering that occurred during the traversal of the object. Digital image enhancement techniques, often referred to as signal recovery, have reached high levels of development. The enhancement of pictures from deep space produced by the Voyager

spacecraft is a typical example. A wealth of references and methodologies are presented in the January 1987 issue of the Journal of the Optical Society of America A, Vol. 4, Number 1, dedicated to Signal Recovery techniques.

A variety of sequences of movements of bundles 5 and/or 8 may be carried out, depending on the purpose of the examination. Two examples will now be given.

The first example is a broad screening search for regions of possible anomaly.

The bundles 5 and 8 will normally be clamped or coupled together to give a fixed angle between them (preferably for forward scattering). Then bundle 5 would be moved over the object surface, with bundle 8 remaining in contact with it. With bundle 8 remaining at a fixed angle to and at a fixed separation from bundle 5, it would not necessarily be moved, but if desired it can be allowed to move over a limited area.

For an additional or alternative more detailed screening, a suspect sub-volume of the object will be concentrated on by directing bundle 5 (always coupled to the object) so that its beam passes through that sub-volume. With bundle 5 held stationery, bundle 8 will be moved over most of the surface whilst orientating it to receive directly scattered radiation from the sub-volume. Bundle 5 would then be moved to another position again directed at the same sub-volume, and bundle 8 would be scanned as before. This process may be repeated as desired for various positions of bundle 5 directed at the required sub-volume. Computer processing of the various results from that sub-volume gives characterisation of inhomogeneities within the sub-volume causing spatial variations of the detected intensity values.

The described embodiment achieves its measurements in sharp contrast to prior art. This is most easily seen in the consideration of the preferred embodiments for the examination of human breast tissue. Mammographic and diaphanographic methods illuminate the entire breast or a reasonably large fraction of it. The present embodiment concentrates on fine beam illumination of a small region within the breast and a collimated detection thereof. Prior art generally measures radiation (x-ray or light) passing straight through the breast. The present embodiment emphasizes the ability to examine the scattered and transmitted radiation at many angles of observation with respect to a defined volume within the breast. In addition, in contrast to diaphanography, the present embodiment emphasizes the need to eliminate surface interface effects. As is well known, radiation striking an interface between two surfaces of refractive index n_1 and n_2, respectively, will reflect back from that surface. The fraction of radiation reflected thereby relative thereby relative to the light radiation incident thereon is given, for normal incidence, by

$$R = (n_1 - n_2)^2/(n_1 + n_2)^2$$

For the case of human tissue having a dehydrated value of about $n_1 = 1.5$, the reflection at the skin-air interface will be about 4% where $n_2 = 1.0$, for air. For <u>non</u>-normal incidence, this reflected fraction increases to 100% at the critical angle

$$0_c = \sin^{-1}(n_2/n_1).$$

For $n_1 = 1.5$ and $n_2 = 1$, $0_c = 41.8°$. This means that any light internal to the breast, in this example, and incident at an angle greater than about 42° with respect to the normal will be completely reflected. Multiple scattering within such semi-opaque objects insures that a great fraction (over 50%) of all light transmitted through, for example, breast tissue will be reflected back into the breast to be further degraded and absorbed. The present embodiment pays particular attention to the need to prevent such surface-induced degradations by coupling the light incident on the air-object interface from within the object to the collection device using refractive index matching fluids 22 as indicated in Fig. 4.

In the absence of multiple scattering, the measurement shown in Figure 6 corresponds to the familiar Fraunhofer scattering configuration. The small particles in region 25 scatter light which is then collected at a great distance from the particles relative to their size. If we wanted to image the objects themselves rather than their Fraunhofer diffraction/scattering patterns, then an imaging lens structure 28 as shown in Figure 7 would be required. This lens structure would form an image 29 of the elements 30, say, within the object 21 at the detector array 11 after collection at 8 and intensity amplification at 9. The optical fiber coupling 10 shown between the image intensifier plate 9 and array 11 of Figure 2 would now include intermediate lens structure 28. Standard optical tracing rays are indicated by 31 and 32, respectively. The lens structure 28 or other lens elements may also be placed in front of collection bundle 8 or between other indicated elements of the collection device so that the resulting image would be optimised for the wavelength and object elements examined. Care to couple all such lens elements as discussed hereinbefore should be exercised at all times.

As will be seen from the information hereinbefore disclosed, there are many modifications and variations of the preferred embodiments discussed that will serve the purpose of the invention equally well. All such modifications and variations are included herein, and form obvious extensions thereof.

Optional inventive aspects not all specifically referred to in the claims also concern the following features taken single or in combination.

1. When a laser is used it is a He-Ne laser
   1a. The laser produces red light, or
   1b. The laser produces infrared light
2. The light amplification means is a microchannel plate.
   2a. The plate is a chevron plate, or
   2b. The plate is a C-plate, or
   2c. The plate is a Z-plate.
3. The refractive index matching means is a fluid.

Claims

1. A method of examining the interior of a semi-opaque object with light, the method comprising:

coupling a collimated beam of light to a first surface portion of said body;

collecting light scattered within said body at a further surface portion of the body;

amplifying the collected light whilst substantially preserving its spatial intensity variations;

converting pixels of the amplified light into electrical data signals which are passed to computer means for storage therein;

processing the resulting data on the computer means to characterise the region of the object causing spatial variations in the collected light;

repeating the processing for different orientations of the incident and/or collected light.

2. A method for the examination of the interior of a semi-opaque object comprising the following steps:

A. Forming a narrow, collimated beam of light;

B. Coupling said beam of light onto the semi-opaque object (21) at a desired entrance surface region using a refractive index matching means, thereby coupling said beam of light into said object;

C. Coupling a fraction of said light, scattered within and impinging upon a desired surface exit region of said object from the inside of said object by refractive index matching means to an optical collection means (8) at said surface exit region;

D. Coupling said optical collection means (8) into a light amplification means (11) which preserves the spatial intensity variations incident thereon and collected at said surface exit region by said optical collection means;

E. Impinging the amplified light on an array (13) of photodetectors;

F. Converting each detected intensity corresponding to each detector element of said array (13) into a numerical value and transmitting each such value into a memory means (16b);

G. Processing and analysing said numerical values in said memory means by computer means (18) and characterizing thereby the region of said examined object causing the spatial variation of said intensity values.

3. A method according to claim 2 comprising:

H. Repeating said measurements at different orientations of said incident coupled light;

I. Varying said entrance and/or exit surface region and repeating steps G & H; and

J. Characterizing thereby the inhomogeneities within said semi-opaque object causing the spatial variations of said detected intensity values.

4. A method according to claim 1, 2 or 3, and comprising passing the formed beam into a lens (2), said lens focusing said beam into an optical fiber means (3), said optical fiber means terminating at the focal point of a second lens (4), and said second lens coupled into an optical fiber coupling device (5).

5. A method according to claim 4, wherein the lenses are half pitch gradient refractive index lenses.

6. A method according to any one of the preceding claims, wherein said beam of light is substantially monochromatic.

7. A method according to claim 6 wherein the beam of light is from a laser (1).

8. A method according to claim 7 wherein the laser light is linearly polarized.

9. A method according to claim 7, wherein the laser light is unpolarized.

10. A method according to any one of the preceding claims, where the light amplification means (10) is a microchannel plate.

11. A method according to any one of the preceding claims, wherein the array of photodetectors (13) comprises photodiodes.

12. A method according to any one of claims 1 to 10, wherein the array of photodetectors (13) forms a charge coupled device.

13. A method according to any one of the preceding claims wherein the semi-opaque object is a human breast.

14. A method according to any one of the preceding claims, wherein said amplified light is made to impinge upon a lens element before impinging on said array of photodetectors forming, thereby, an image of a region interior to said object on said photodetector array.

15. A method according to any one of the preceding claims, wherein the processing of said numerical values includes the process of signal recovery or enhancement.

16. A method according to any one of the preceding claims, wherein the orientations and positions of the elements coupled to the semi-opaque object being examined are measured.

17. A method according to claim 16, wherein the measurements derived therein are used to calculate the path through the semi-opaque object.

18. A method according to claim 16 or 17, wherein the measurements derived therein are used to calculate the locations of the scattering objects therewithin and the angle of scattering therefrom with respect to the direction of the incident light.

19. A method according to any one of the preceding claims and including processing and analysing the collected numerical values so as to determine the degree of coherence in said collected values.

20. An instrument for the examination of the interior of a semi-opaque object and comprising:

collimated light generating means (1) for providing a beam of light coupling to an entrance surface of said object; and

light collection and processing means (8,10,13) for collecting light from said beam which has scattered within the body and emerged from an exit region thereof;

characterised in that the collection and processing means comprise collection optical fiber means (8) for coupling by refractive index matching means to said exit region, light amplification means (10) for amplifying light from said collection optical fiber means (8) while maintaining its spatial variations at said collector optical fiber means (8), photodetector array means (13) for converting pixels of the amplified light to electrical signals, analog-to-digital conversion means (16a) for converting said signals to digital form, and computer processing means (16b, 18) for storing and processing said signals in digital form.

21. An instrument for the examination of the interior of a semi-opaque object and comprising:

A. Collimated light means (1) for producing a narrow beam of light;

B. Focusing lens means (2) focusing said collimated light beam on an optical fiber transmitting means (3) terminating at the focal point of a

C. Second lens means (4) imaging said transmitted light to

D. Optical coupling means (5); said optical coupling being for coupling onto the semi-opaque object at a desired entrance surface thereon by refractive index matching means so that said transmitted light incident thereon is coupled into said object at said entrance surface;

E. Collection optical fiber means (8), said fiber means being for coupling by refractive index matching means to an exit surface region of said object through which light scattered within said object has scattered thereto;

F. Light amplification means (10) whereby light collected from solid object in step E is amplified in intensity while maintaining its spatial variations at said collector optical fiber plate means;

G. Photodetector array means (13) for producing from the amplified light output signals proportional to incident intensities;

H. Analog-to-digital conversion means (16) for converting each signal at each photodetector element in said photodetector array means into a digital representation; and

I. Computer processing means for receiving said digital representation.

22. An instrument according to claim 20 or 21, wherein optical lens means (28) as provided to image the amplified light spatial variations onto the photodetector array means

23. An instrument according to any one of claims 20 to 22, wherein said collimated beam of light is substantially monochromatic.

24. An instrument according to any one of the preceding claims wherein the collimated light means (1) is a laser.

25. An instrument according to claim 24, and arranged to provide laser light which is linearly polarized.

26. An instrument according to claim 24, and arrange to provide laser light which is unpolarized.

27. An instrument according to any one of claims 20 to 26 wherein the lens means are provided by half pitch gradient refractive index lenses.

28. An instrument according to any one of claims 20 to 27, wherein the light amplification means is a microchannel plate.

29. An instrument according to any one of preceding claims wherein the array of photodetectors comprise photodiodes.

30. An instrument according to any one of claims 20 to 28, wherein the array of photodetectors is provided by a charge coupled device.

31. An instrument according to any one of claims 20 to 30 wherein said computer processing means includes means for the process of signal recovery or enhancement.

32. An apparatus for producing a near parallel, spatially homogeneous, unpolarized laser beam from a spatially inhomogeneous laser beam, comprising a half pitch gradient refractive index lens joined on its central axis to an optical fiber which, in turn, is joined to substantially identical gradient refractive index lens.

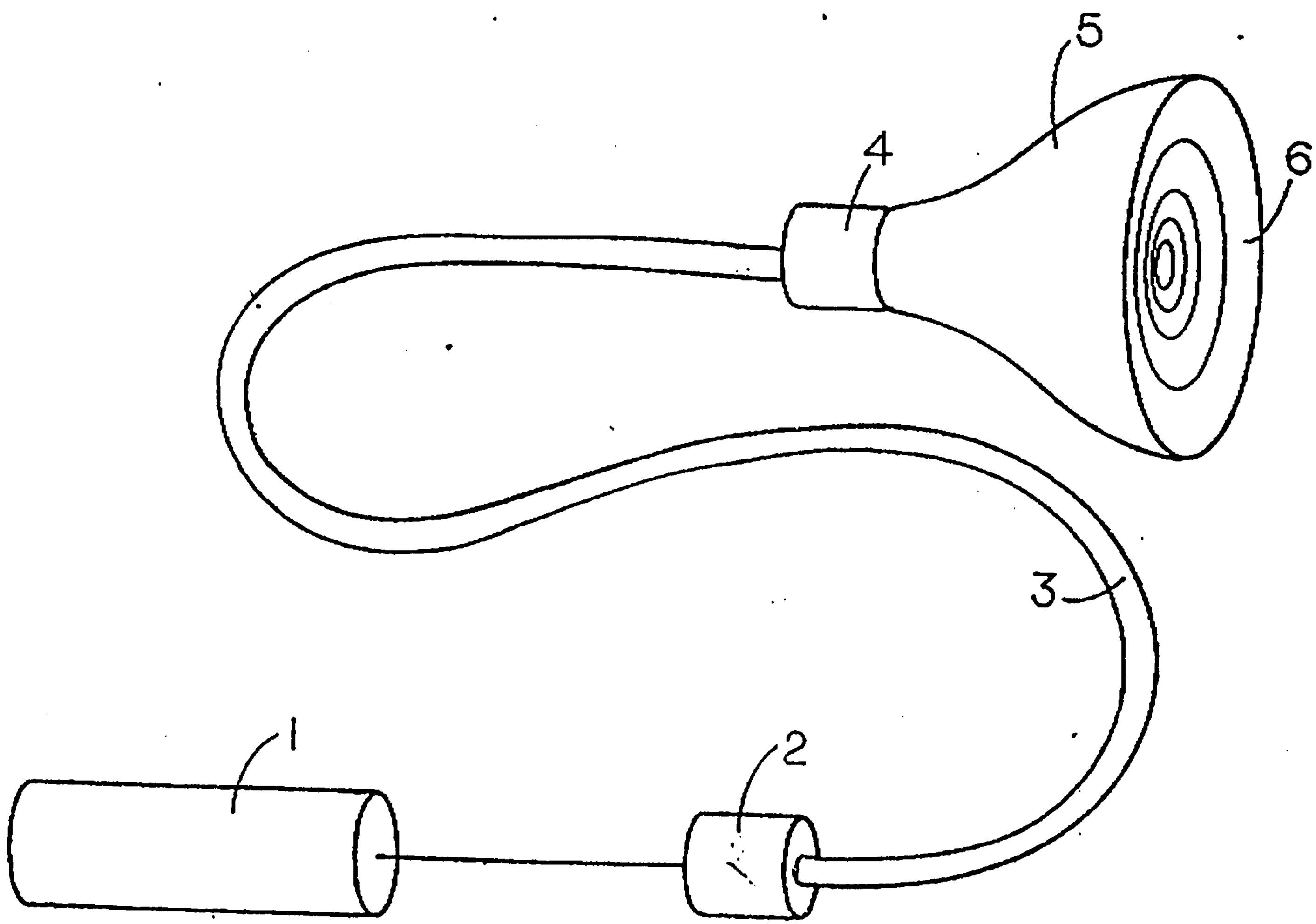

FIGURE 1

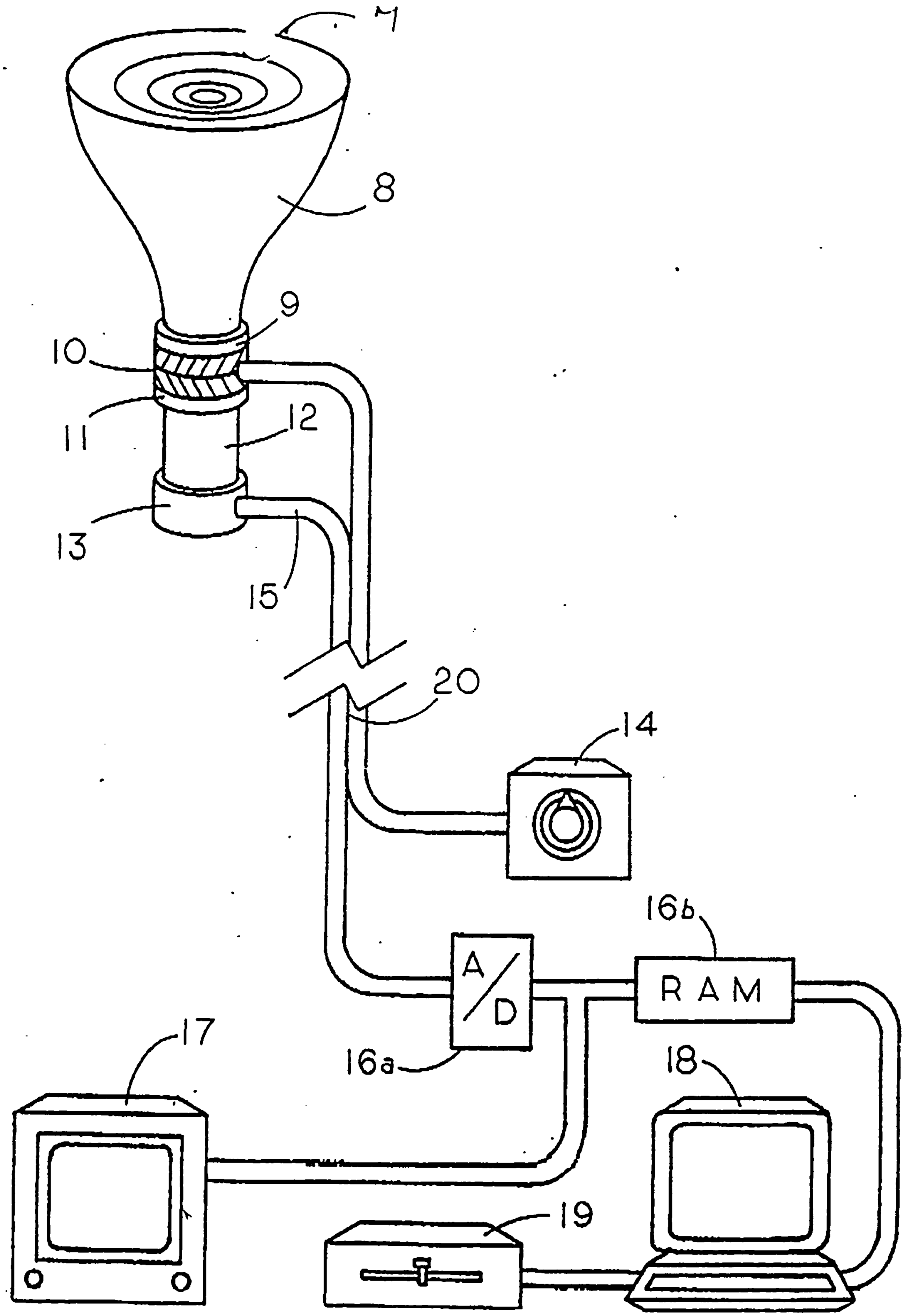

FIGURE 2

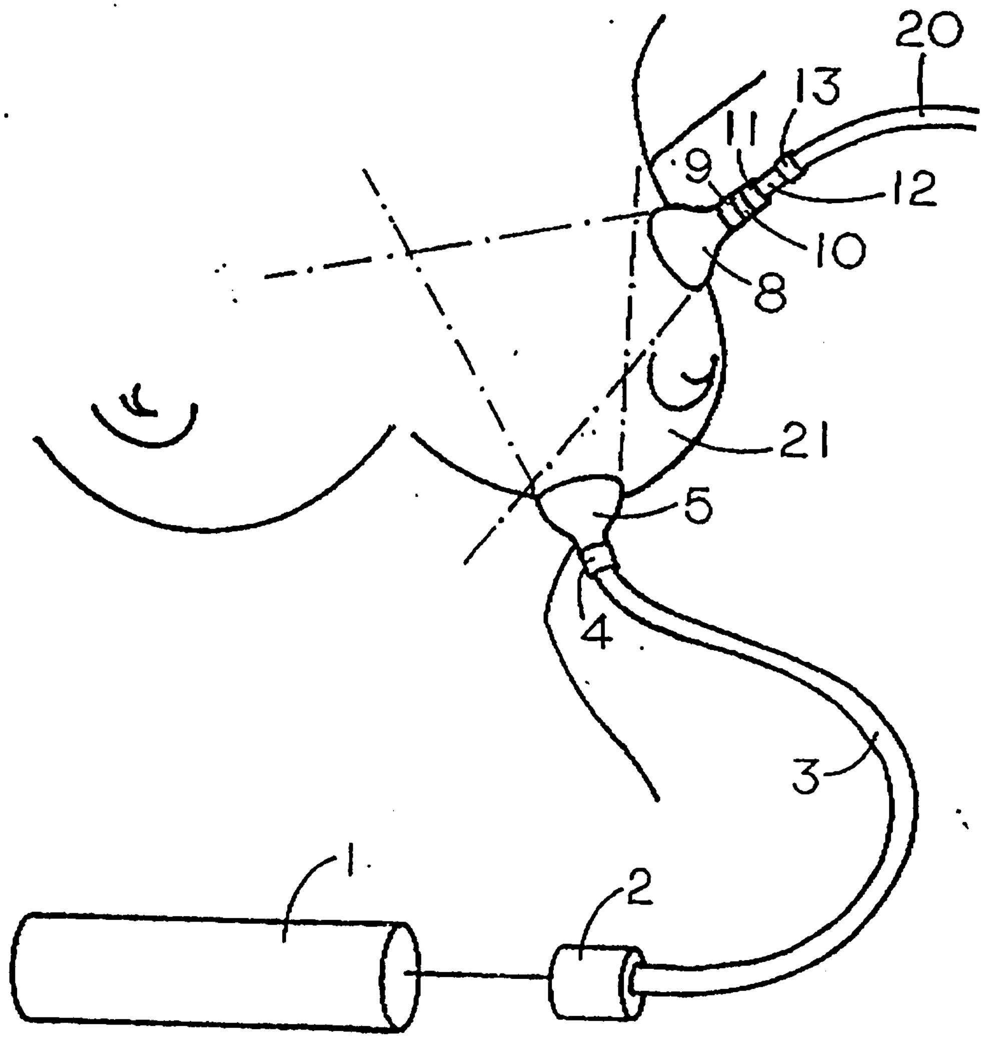

FIGURE 3

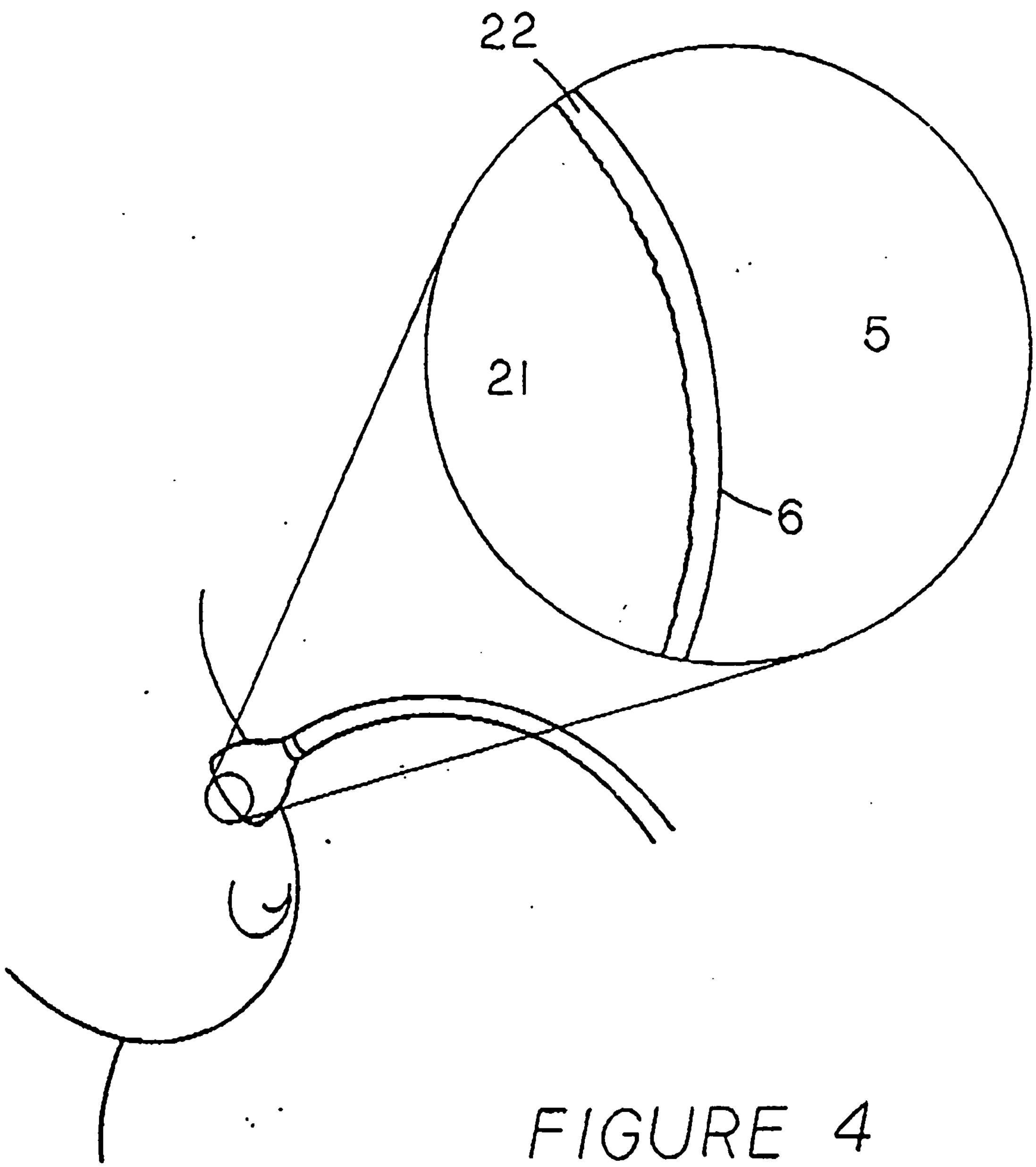

FIGURE 4

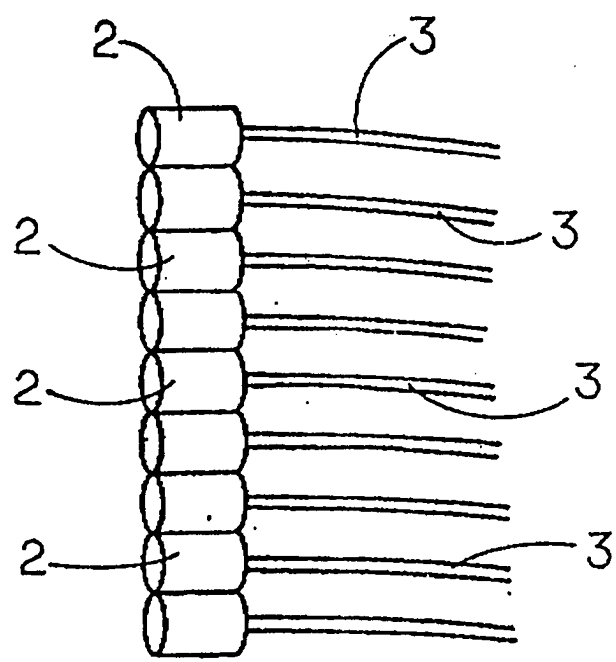

FIGURE 5

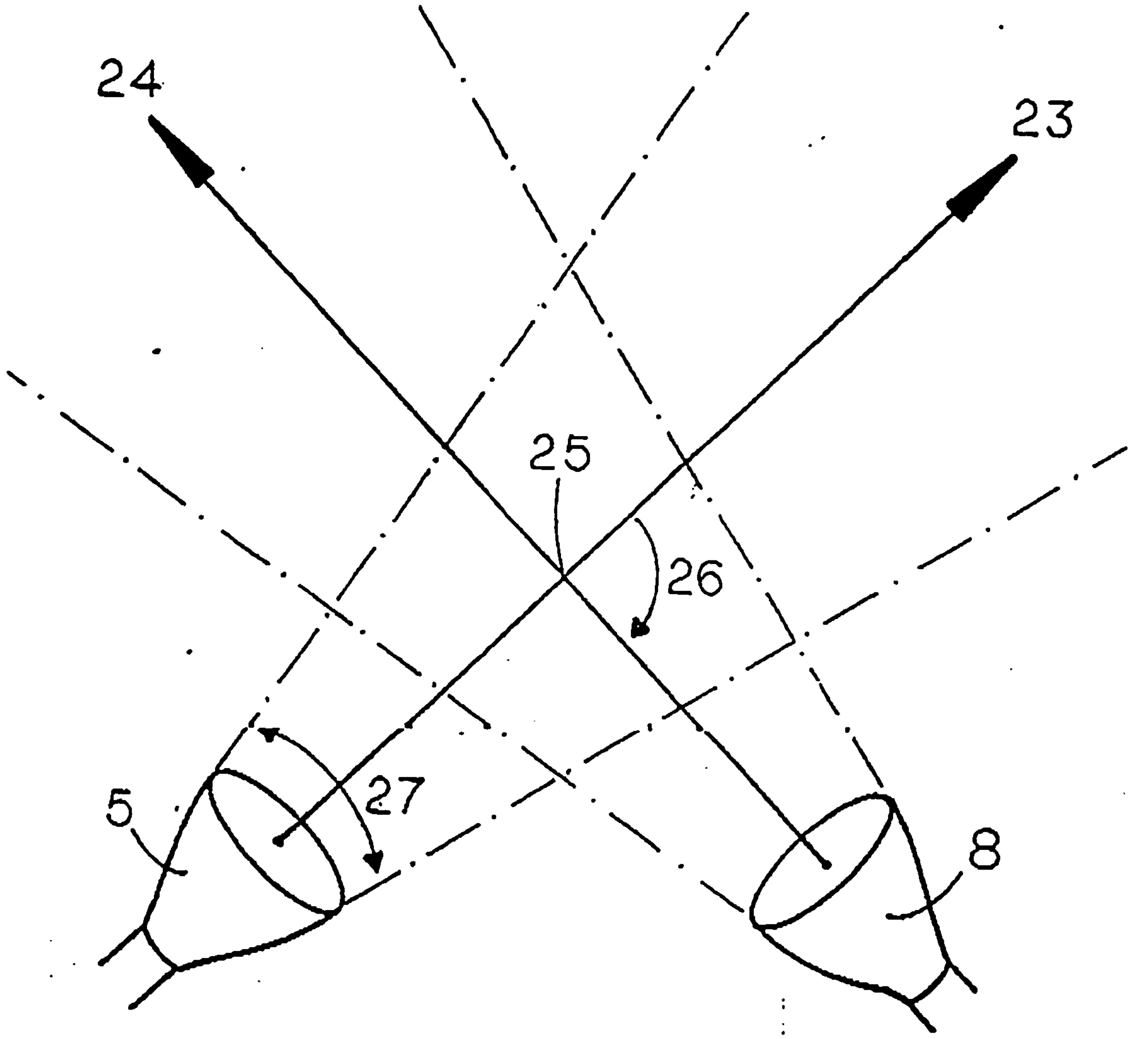

FIGURE 6

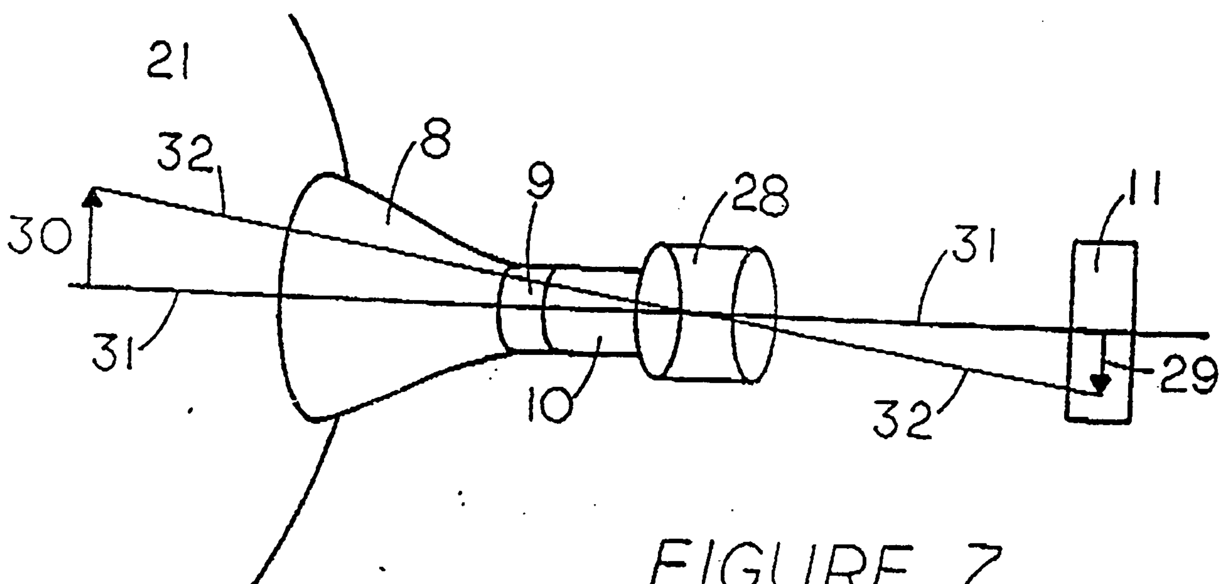

FIGURE 7

European Patent Office

EUROPEAN SEARCH REPORT

Application Number

EP 88 30 0882

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.4)
X	IBM TECHNICAL DISCLOSURE BULLETIN, vol. 27, no. 12, May 1985, pages 6971-6973, New York, US; "Inspection system for particulate and defect detection on product wafers" * The whole article *	1,7,16-18,24	A 61 B 5/00 G 01 N 21/47
Y	US-A-4 555 179 (J.LANGERHOLC et al.) * The whole document *	1-3,7,14,20-22,24	
A		11,29	
Y	GB-A-2 126 717 (HAMAMATSU PHOTONICS K.K.) * Abstract; page 2, line 98 - page 3, line 79; figures 2,6,7 *	1-3,7,14,20-22,24	
A		4,6,10,23,28	
A	APPLIED OPTICS, vol. 22, no. 15, 1st August 1983, pages 2241-2242, New York, US; E.M.VOGEL: "Method of characterizing the optical quality of glass" * The whole article *	1-4,6,7,20,21,23,24	TECHNICAL FIELDS SEARCHED (Int. Cl.4) A 61 B G 01 N G 02 B G 06 F
A	US-A-4 651 744 (D.L.BRISTOW et al.) * Column 1, lines 5-22; column 3, line 15 - column 4, line 25; figure 1 *	1,2,13,20,21	
A	FR-A-1 513 676 (F.P.BUSSER) * Page 1, left-hand column, lines 1-40; page 2, right-hand column, lines 43-51 *	6,13,23	

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
THE HAGUE	02-05-1988	FERRIGNO, A.

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document